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Polysaccharides and Natural Gums for Colon Drug Delivery

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The site-specific delivery of the drugs to the target sites has the potential to reduce the side effects and improved the pharmacological response. The colon drug targeting is also exploited for systemic delivery of active drugs. For colonic drug delivery, many physiological barriers must be overcome, the major one being absorption or degradation of the active drugs in the upper part of the GIT-Tract. Natural polymers particularly in the form of microspheres, have an important role in the before they will have widespread use in clinical situations. Among these issues are better understanding of the kinetics of drug release; more effective ways to control burst phenomena; greater understanding of drug-polymer interactions and their effect on shelf life stability; additional animal studies to determine local tissue response, biodegradation rates, and metabolic rate. Well-designed Clinical studies to assess efficacy in relation to current therapies.

Keyword: Polysaccharides, Colon Drug Delivery, Pectin

INTRODUCTION: The colon is attracting interest as a site where poorly absorbed drug molecule may have an improved bioavailability. This region of the colon is recognized as having a somewhat less hostile environment with less diversity and intensity of activity than the stomach and small intestine. Oral delivery of drugs to the colon is valuable in the treatment of diseases of colon (ulcerative colitis, Crohn's disease, carcinomas and infections) whereby high local concentration can be achieved while minimizing side effects that occur because of release of drugs in the upper GIT or unnecessary systemic absorption. The colon is rich in lymphoid tissue, uptake of antigens into the mast cells of the colonic mucosa produces rapid local production of antibodies and this helps in efficient vaccine delivery. The colon has a longer retention time and appears highly responsive to agents that enhance the absorption of poorly absorbed drugs.The simplest method for targeting of drugs to the colon is to obtain slower release rates or longer releaseperiods by the application of thicker layers of conventional enteric coatings or extremely slow releasing matrices.

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Pectin: Pectins are nonstarch linear polysaccharides that consist of α-1, 4 D-galacturonic acid and 1, 2 D-rhamnose with D-galactose and D-arabinose side chains having average molecular weights between 50,000 to 150,000. Pectin tends to produce lower viscosities

than other plant gums. It is refractory to host gastric and small intestinal enzymes but is almost completely degraded by the colonic bacterial enzymes to produce a series of soluble oligalactorunates [1]. Depending on the plant source and preparation; they contain varying degrees of methyl ester substituents [2]. Micro particulate polymeric delivery systems have been suggested as a possible approach to improve the low bioavailability characteristics shown by standard ophthalmic vehicles (collyria). In this context pectin microspheres of piroxicam were prepared by the spray drying technique. In vivo tests in rabbits with dispersions of piroxicam-loaded microspheres also indicated a significant improvement of piroxicam bioavailability in the aqueous humour (2.5-fold) when compared with commercial piroxicam eye drops [3, 4]. In vivo gamma scintigraphic studies confirmed the in vitro findings. In all the volunteers, the pectin-coated tablets disintegrated in the colon indicating that site-specificity had been achieved and illustrating the potential of a colonic drug delivery system utilizing pectin. This necessitates the development of such derivatives of pectin, which were less water-soluble but were having the capability to be degraded by the colonic microflora. Calcium pectinate, the insoluble salt of pectin was used for colon targeted drug delivery of indomethacin by Rubeinstein et al. [5]. The results suggest that the pectin-chloroquine patch matrix preparation has potential applications for the transdermal delivery of chloroquine and perhaps in the management of malaria. Calcium pectinate nanoparticles to deliver insulin were prepared as a potential colonic delivery system by ionotropic gelation [6].

Chitosan: Chitosan is a high molecular weight polycationic polysaccharide derived from naturally occurring chitin by alkaline deacetylation. Chemically, it is a poly (N-glucosamine). Chitosan has favorable biological properties such as nontoxicity, biocompatibility and biodegradability. Similar to other polysaccharides it also undergoes degradation by the action of colonic microflora and hence poses its candidature for colon targeted drug delivery. Therapeutic effect of R-68070, a new thromboxane synthetase inhibitor on 2,4,6 trinitrobenzene sulfonic acid sodium salt induced ulcerative colitis was studied using chitosan capsules to achieve its colon-specific drug delivery in rats [7]. A multiparticulate system of chitosan hydrogel beads has been investigated for colon-specific drug delivery of macromolecules using fluorescein isothiocanate-labeled bovine serum albumin as a model protein. The hydrogel bead was formed by polyelectrolyte complexation of chitosan with its counter ion, tripolyphosphare. The protein release experiments were carried out in vitro under different conditions to simulate the pH and times likely to be encountered during intestinal transit to the colon. The results shown that the hydrogel beads were degraded by rat cecal and colonic enzymes, resulting in a marked acceleration in the release of protein [8]. Chitosan microspheres are used to provide controlled release of many drugs and to improve the bioavailability of degradable substances such as protein, as well as to improve the uptake of hydrophilic substances across the epithelial layers. These microspheres are being investigated both for parenteral and oral drug delivery [9].

GUMS:

Gums are translucent and amorphous substances produced by the plants. Usually pathological products, gums are produced when the plant is growing under unfavorable conditions or when injured. Gums are plant hydrocolloids and may be anionic or non ionic polysaccharides. On

hydrolysis gums yield sugar and salts of uronic acid [10].

Guar gums: It is a naturally occurring galactomannan polysaccharide; consists of chiefly high molecular weight hydrocolloidal polysaccharide, composed of galactan and mannan units combined through glycosidic linkages and shows degradation in the large intestine due the presence of microbial enzymes [11]. Guar gum is hydrophilic and swells in cold water, forming viscous colloidal dispersions or sols. This gelling property retards release of the drug from the dosage form, making it more likely that degradation will occur in the colon. Guar gum was found to be a colon-specific drug carrier in the form of matrix and compression-coated tablets as well as microspheres [11]. Guar gum-based matrix tablets of rofecoxib were prepared for their intended use in the chemoprevention of colorectal cancer [12].

Locust Bean Gum: It is also called carob gum, as it is derived from carob (Ceratonia siliqua) seeds. This neutral polymer is only slightly soluble in cold water; it requires heat to achieve full hydration and maximum viscosity. Cross-linked galactomannan however led to water-insoluble film forming product-showing degradation in colonic microflora [13].

Karaya gum: Karaya gum is obtained from Sterculia urens (Family sterculiaceae) is a partially acetylated polymer of galactose, rhamnose, and glucuronic acid [13]. Park et al. showed that mucoadhesive tablets prepared by karaya gum for buccal delivery, had superior adhesive properties as compared to guar gum and was able to provide zero-order drug release, but concentrations greater than 50 % w/w may be required to provide suitable sustained release [15].

Albizia gum: Albizia gum is obtained from the incised trunk of the tree Albizia zygia (DC) J. F. Macbr, family Leguminosae and is shaped like round elongated tears of variable color ranging from yellow to dark brown. It consists of β-1– 3-linked D-galactose units with some ß1-6-linked Dgalactose units. The genus Albizzia containing some twenty-six species is a member of the Mimosacez, a family which also includes the gum-bearing genera Acacia and Prosopis. Only two species of Albizia, A. zygia and A. sassa, are however, known to produce gum. Albizia gum has been investigated as a possible substitute for gum Arabic as a natural emulsifier for food and pharmaceuticals [16, 17].

Xanthan gum: Xanthan gum is a high molecular weight extra cellular polysaccharide produced by the fermentation of the gram-negative bacterium Xanthomonas campestris. The anionic character of this polymer is due to the presence of both glucuronicacid and pyruvic acid groups in the side chain [18]. In one of the trials, xanthan gum showed a higher ability to retard the drug release than synthetic hydroxyproylmethylcellulose. Xanthan gum and hydroxypropylmethylcellulose were used as hydrophilic matrixing agents for preparing modified release tablets of diltiazem HCl. The amount of hydroxypropylmethylcellulose and xanthan gum exhibited significant effect on drug release from the tablets prepared by direct compression technique. It was concluded that by using a suitable blend of hydroxypropylmethylcellulose and xanthan gum desired modified drug release could be achieved [19].

Starches: It is the principal form of carbohydrate reserve in green plants and especially present in seeds and underground organs. Starch occurs in the form of granules (starch grains), the shape and size of which are characteristic of the species,

as is also the ratio of the content of the principal constituents, amylose and amylopectin. A number of starches are recognized for pharmaceutical use. These include maize (Zea mays), rice (Oryza sativa) , wheat (Triticum aestivum), and potato (S olanum tuberosum) [20]. To deliver proteins or peptidic drugs orally, microcapsules containing a protein and a proteinase inhibitor were prepared. Starch/bovine serum albumin mixed-walled microcapsules were prepared using interfacial cross-linking with terephthaloyl chloride. The microcapsules were loaded with native or amino-protected aprotinin by incorporating protease inhibitors in the aqueous phase during the cross-linking process. The protective effect of microcapsules with aprotinin for bovine serum albumin was revealed in vitro [21].

Alginates: Alginates are linear polymers that have 1-4'linked β-D-mannuronic acid and α-L-guluronic acid residue arranged as blocks of either type of unit or as a random distribution of each type. A Eudragit L-30D–coated calcium alginates bead for colonic delivery of 5-aminosalicylic acid has been reported [22]. Different enteric as well as sustained release polymers were applied as coat on calcium alginate beads. A system was prepared by coating calcium alginate beads with Aquacoat® that is a pH-independent polymer followed by 2 % w/w coating of Eudragit L-30D. Being enteric polymer, Eudragit® resisted the release of drug in acidic media and drug release was triggered at alkaline pH and controlled by thickness of Aquacoat®. When drug-loaded calcium alginate beads swell sufficiently (osmotic gradient) to exceed the strength of outer sustained released coat, the film bursts to release the drug. Such a system delivers drug to the distal intestine with minimal initial leak and provides sustained release in the colon [23].

Inulin: Insulin is a naturally occurring storage polysaccharide found in many plants such as onion, garlic, artichoke, and chicory. Most of these fructose chains have a glucose unit as the initial moiety. It is not hydrolyzed by the endogenous secretions of the human digestive tract [24]. However, bacteria harboring in the colon and more specifically Bifidobacteria are able to ferment inulin [25].

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